

Supplementary Material

Lewis acid-catalyzed Diels-Alder reaction of 2-cyclopentenones with Danishefsky's diene: double bond isomerization of tetrahydro-1*H*-indene-1,5(7*aH*)-diones, and attempts on an asymmetric catalysis

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Dedicated to Prof. Rainer Beckert on the occasion of his 60th birthday

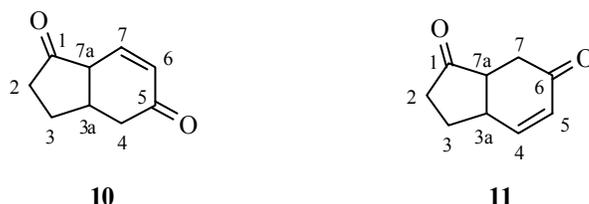
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NMR-spectroscopic analysis of the inseparable double bond isomers **10**, **12**

The NMR-spectroscopic analysis of the isolated mixture of double bond isomers **10** and **12** is discussed in the following:

Initially we expected the two compounds to be the two regioisomers **10** and **11** as shown below.



Scheme S1

If indeed the regioisomers **10** and **11** were formed, we should have found a multiple degenerated doublet in the range of 5 and 7 ppm in the $^1\text{H-NMR}$ spectrum for each of the vinylic protons 6-H and 7-H (regioisomer **10**) and 4-H and 5-H (regioisomer **11**) respectively. As shown in the enlargement of the olefinic part of the $^1\text{H-NMR}$ spectrum between 5.80 and 6.35 ppm in Figure S1, the NMR experiment provided a doublet of doublets ($J = 10.1$ Hz, $J = 2.6$ Hz) at 5.84 ppm and a doublet of doublets of doublets ($J = 10.1$ Hz, $J = 4.2$ Hz, $J = 0.7$ Hz) at 6.24 ppm. The third multiplet at 6.33 ppm was identified to be a triplet of doublets of doublets ($J = 3.7$ Hz, $J = 3.2$ Hz, $J = 0.7$ Hz). The integration of the triplet of doublets of doublets showed a value of one whereas the doublet of doublets of doublets and the doublet of doublets contained an integration of 0.75 each. This and the fact that both had an identical coupling constant (10.1 Hz) led us to the assumption that these two protons are located in the same molecule. The triplet of doublets of doublets was then inevitably assigned to the second compound. On closer examination of the integration we found a ratio of 0.75:1.75 or 0.43:0.57 of the two isomers that is attended by GC analysis (cf. Table 1). Conflicting our first theory of the two regioisomers **10** and **11** was the fact that we found only three signals for the four expected vinylic protons and the presence of nearly equimolar mixtures made us suspicious of the supposed structure of the two isolated products.

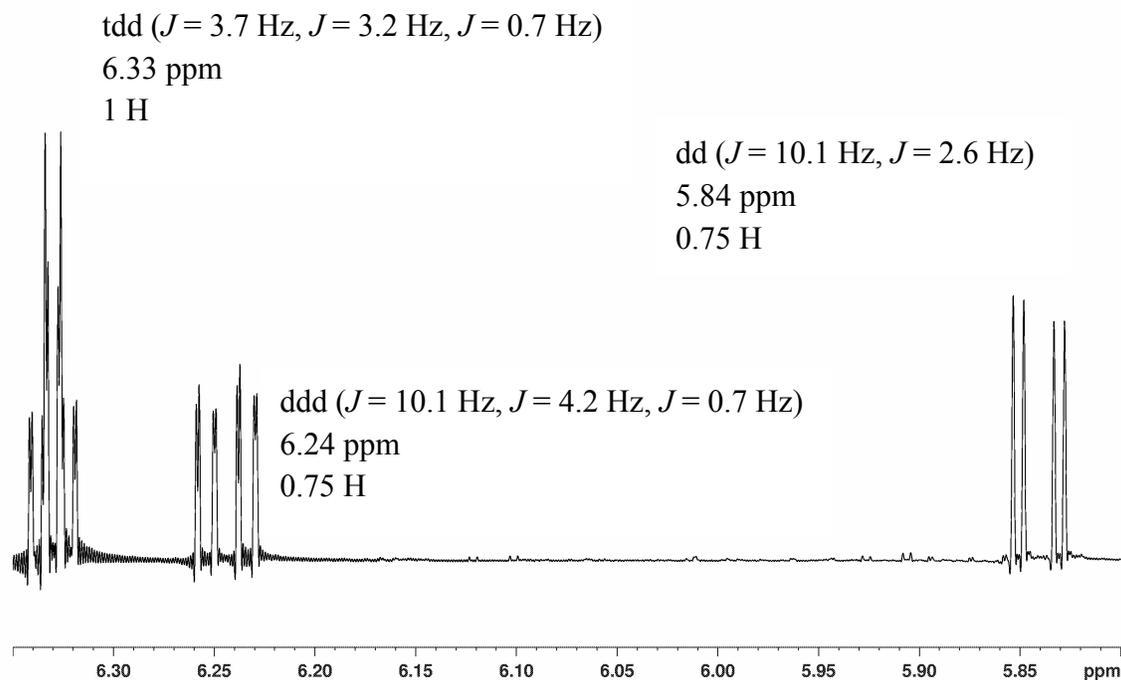


Figure S1 ^1H -NMR spectrum of the inseparable mixture of double bond isomers **10**, **12**

In order to explore the real structures of the two compounds the HSQC spectrum of the mixture was examined carefully. A sector of the HSQC spectrum is shown in Figure S2. One of the carbon atoms (139.3 ppm) in the vinylic part of the spectrum shows no cross peak to any of the protons. Therefore it was assigned as a quaternary carbon. This assumption was confirmed in a DEPT-spectrum that is not shown here.

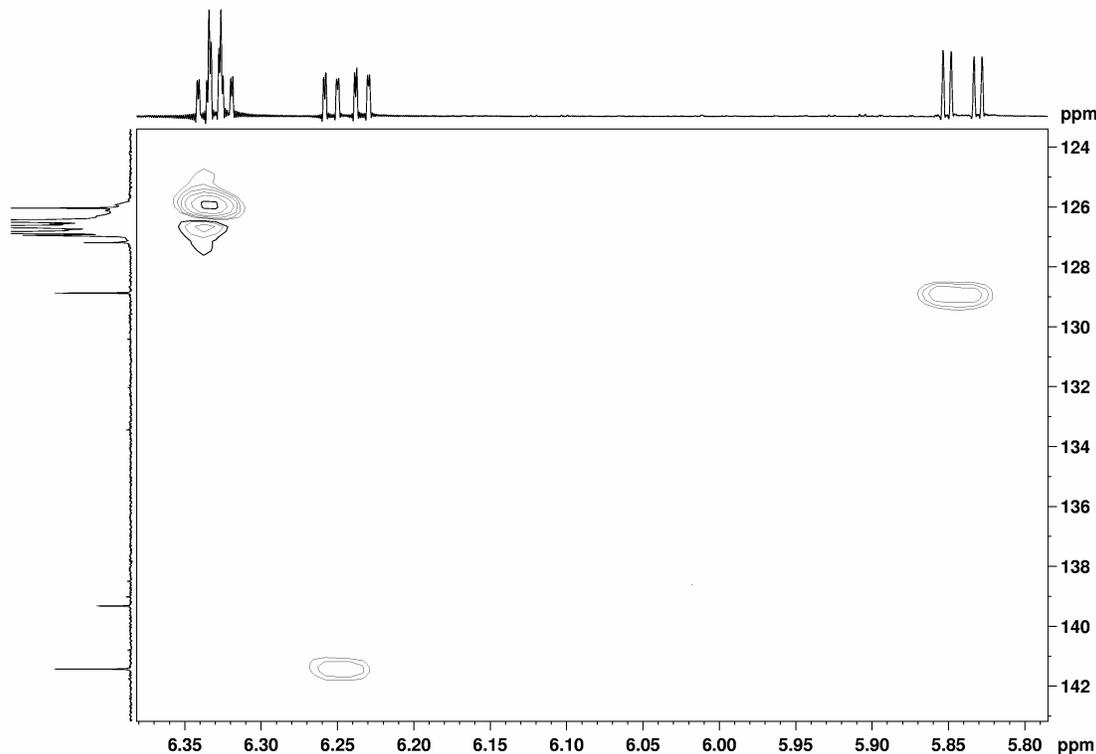
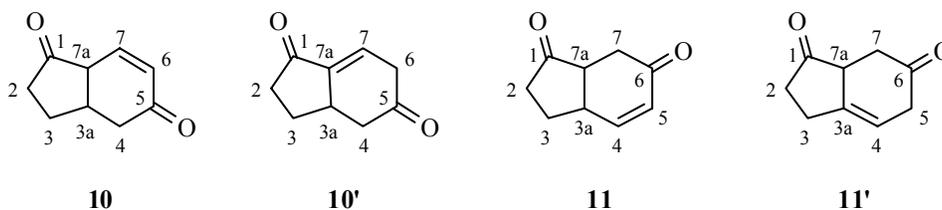


Figure S2 HSQC spectrum of the inseparable mixture of double bond isomers **10**, **12**

At this point it was clear that one of the compounds had a quaternary olefinic carbon atom and owing to the two olefinic protons the other compound had to be one of the two initially expected ones. Altogether there were four possible isomers (Scheme S2).



Scheme S2

The next issue was the position of the double bond. In order to solve that problem, the HMBC spectrum was investigated more closely. Possible correlations between the olefinic protons 6-H and 7-H (isomers **10**, **10'**) and 4-H, 5-H (isomers **11**, **11'**) respectively, and the carbonyl carbon atoms C-1, C-5 (isomers **10**, **10'**) and C-1, C-6 (isomers **11**, **11'**) respectively, should be observed in that spectrum and so the problem of the position of the double bond

should be resolved unambiguously. In the case of isomer **10** there should be a cross peak of the protons 6-H and 7-H to both of the carbonyl C-atoms C-1 and C-5 whereas in the case of isomer **11** the olefinic protons 4-H and 5-H should correlate only to one of the carbonyl C-atoms, namely C-6. The same applies for the isomers **10'** and **11'**. A correlation of the olefinic proton 7-H to both of the carbonyl carbons should be detected in the case of isomer **10'** and only one cross peak should be seen in the case of isomer **11'**. A part of the HMBC spectrum is shown in Figure S3.

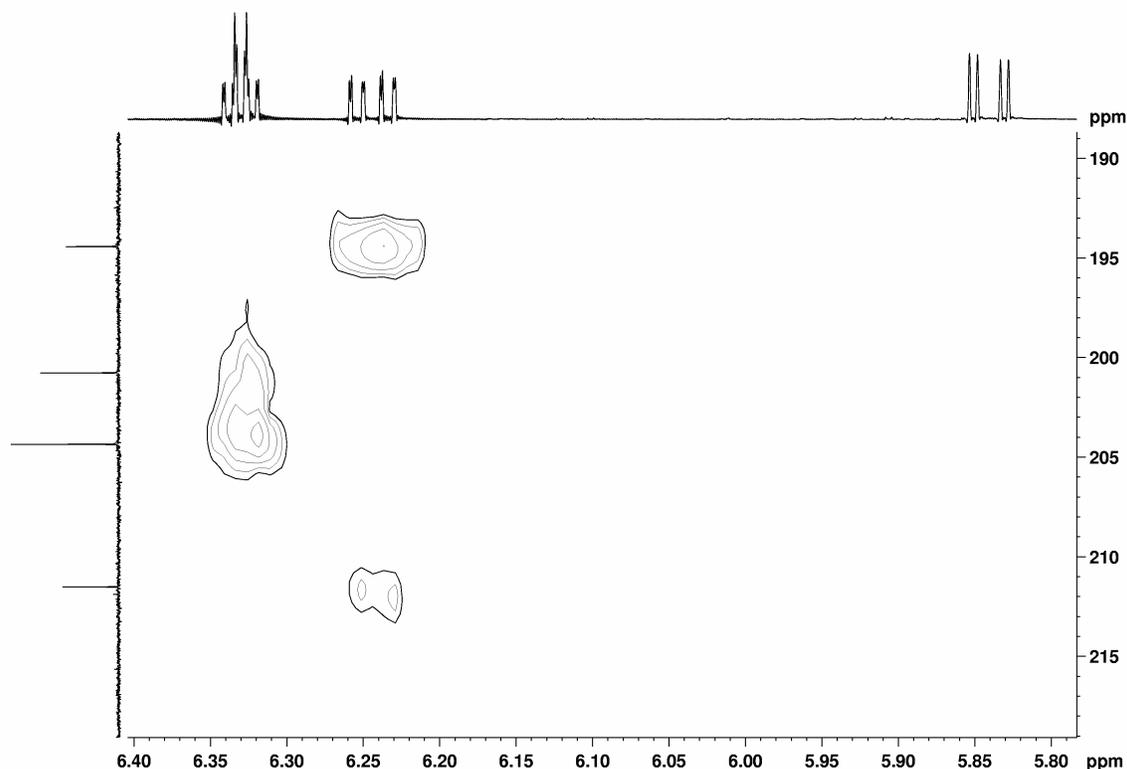
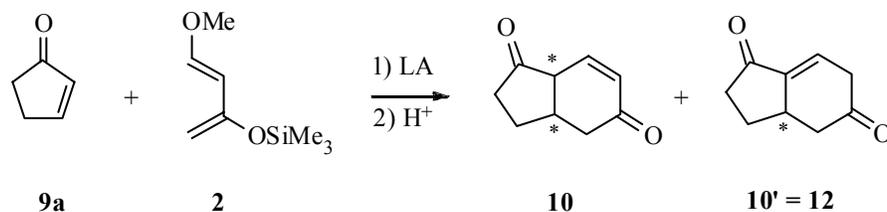


Figure S3 HMBC spectrum of the inseparable mixture of double bond isomers **10**, **12**

The olefinic protons at 6.24 ppm (ddd) and 6.33 ppm (tdd) are unambiguously correlated to two C-atoms. This verifies the structure of the two double bond isomers, that is about the two compounds **10** and **10'** (= **12**) (Scheme S3). It is not uncommon that there is no correlation in the HMBC-spectrum between the dd at 5.84 ppm and the carbonyl C-atoms, since such two-bond-couplings are not always visible in these HMBC spectra.¹



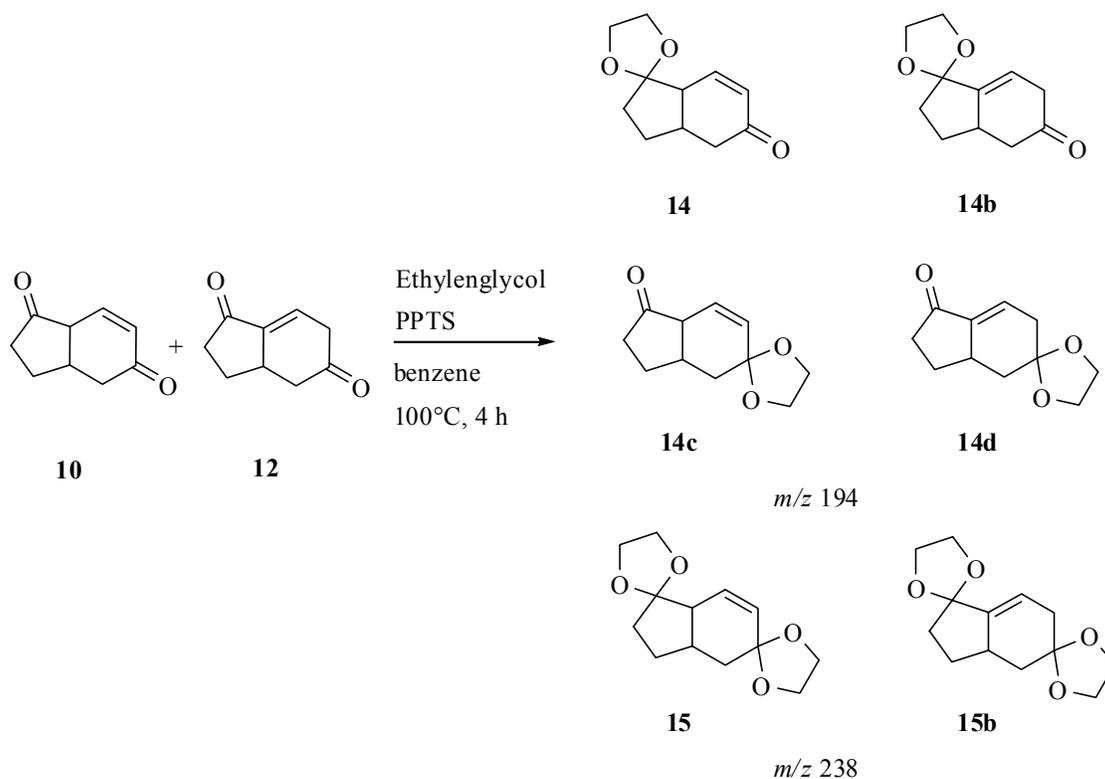
Scheme S3

This result also explains why there was obtained only one product in the selective reduction of the enone moiety.

Details on the isolation of ketals 14, 15

In the following the isolation of the pure monoketal **14** and diketal **15** and their NMR spectroscopic analysis is specified:

As described in the main part the obtained monoketal **14** and the bisketal **15** could not be separated by chromatography (Scheme S4). But initially the structure of the two isolated products (one with m/z 194, the other with m/z 226) was not confirmed – at least four different monoketals **14** – **14d** and two different diketals **15**, **15b** were possible (Scheme S4).



Scheme S4

We felt confident that after reduction of the enone moiety of the monoketal to the corresponding alcohol, the remaining diketal could be separated from the resulting alcohol. The mixture of the monoketal and diketal was reduced with 4 equiv. NaBH_4 in the presence of 0.5 equiv. LiClO_4 in CH_3CN .² Actually we obtained after reduction a mixture of diketal and diastereomeric allylic alcohols (Scheme S5). The desired diketal could then be separated via preparative HPLC and analyzed in NMR experiments. The NMR sample, dissolved in CDCl_3 , was subjected to another GC-MS analysis and we found out that the compound was not the same anymore than before the NMR experiment: Under the slightly acid conditions of CDCl_3 one of the ketal protecting groups was cleaved off. This resulting monoketal showed exactly the same retention time as the monoketal gained during the first ketalization and so we assumed that the two monoketals had the same structure. There is shown the olefinic section of the resulting ^1H -NMR of the obtained monoketal in Figure S4.

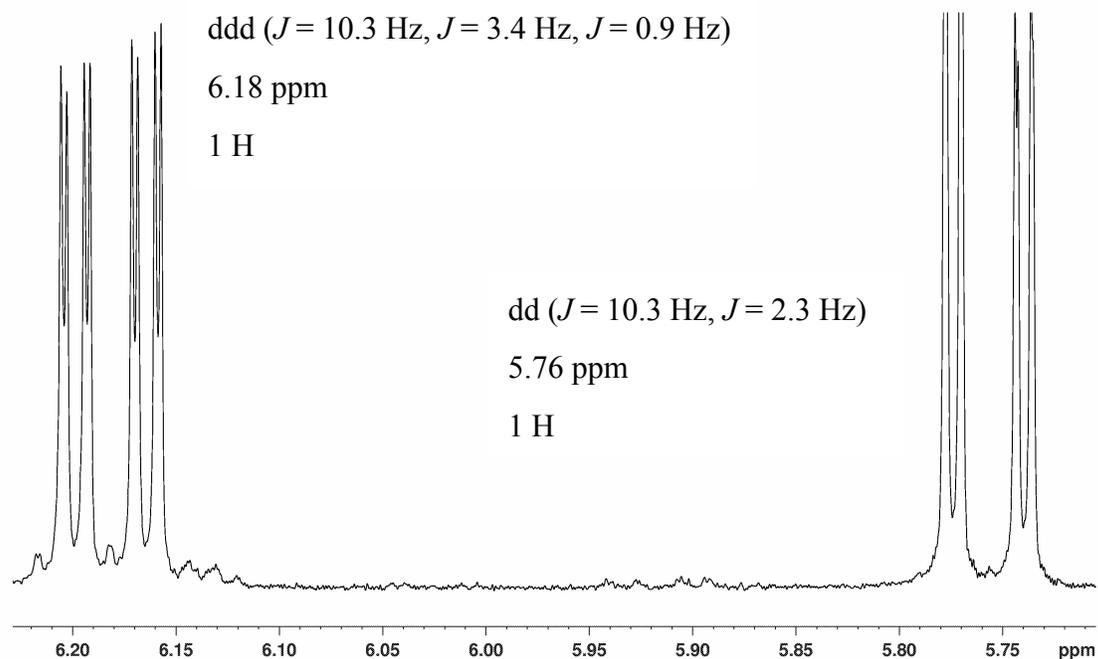
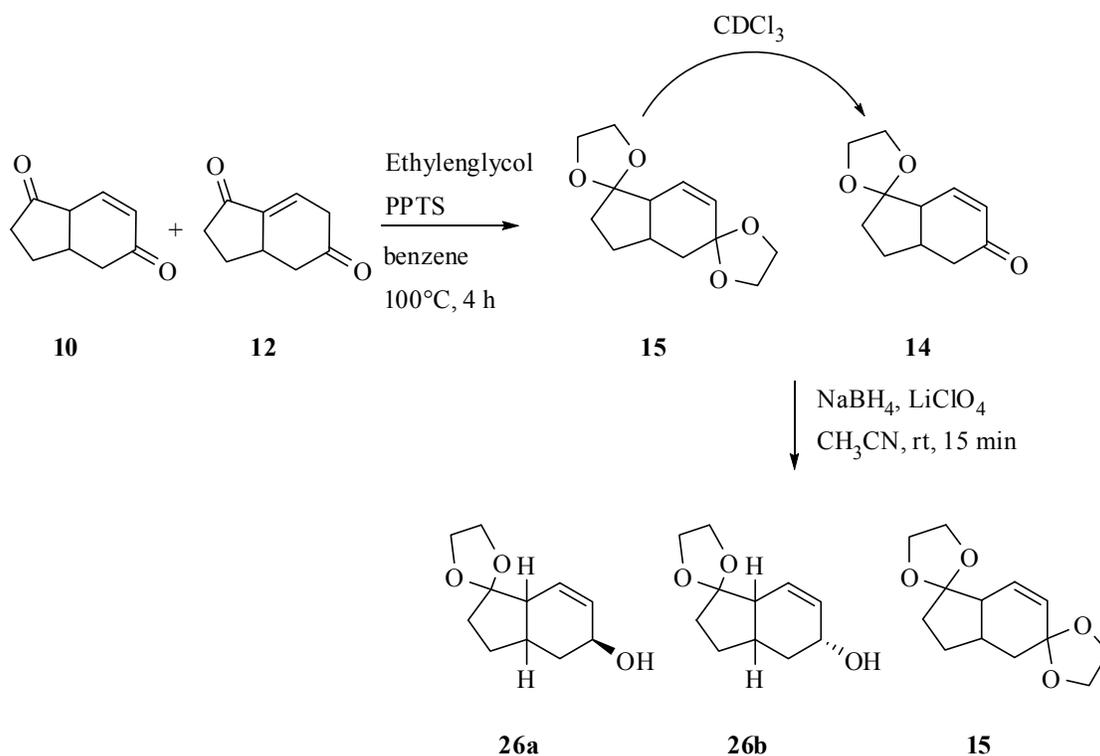


Figure S4 ^1H -NMR spectrum of the obtained monoketal **14**

Comparison of the NMR spectrum with the starting material **10**, **12** revealed that the ketalization took exclusively place with the C6/C7 double bond isomer rather than the C7/C7a isomer. There are visible two signals: One doublet of doublets (5.76 ppm, $J = 10.3 \text{ Hz}, J = 2.3 \text{ Hz}$) and one doublet of doublets of doublets (6.18 ppm, $J = 10.3 \text{ Hz}, J = 3.4 \text{ Hz}, J = 0.9 \text{ Hz}$). The

position of the ketal was determined by comparison of the chemical shifts of the carbonyl carbon in the ^{13}C -NMR spectrum with the ^{13}C -NMR spectrum of the double bond isomer **10**. It is well known that carbonyl carbons in 5-membered rings are detected at lower field (approx. 210-220 ppm) whereas conjugated carbonyl carbons are detected at higher field (approx. 190-200 ppm).³ The double bond isomer **10** shows the carbonyl C-atom in the 5-membered ring at 211.5 ppm whereas the conjugated carbonyl carbon in the 6-membered ring shows up at 194.4 ppm. The carbonyl C-atom in the described monoketal shows one signal at 195.9 ppm. We concluded that the carbonyl carbon must be the one conjugated in the 6-membered ring (Scheme S5).



Scheme S5

The olefinic part of the ^1H -NMR spectrum of the diketal, dissolved in benzene- d_6 is shown in Figure S5. Again a doublet of doublets (5.67 ppm, $J = 10.2$ Hz, $J = 3.1$ Hz) and a doublet of doublets of doublets (5.61 ppm, $J = 10.2$ Hz, $J = 1.6$ Hz, $J = 0.7$ Hz) was observed. Since the difference of the chemical shifts ($\nu_1 - \nu_2$) $\approx J_{1,2}$ the two signals are distorted. Again the similarity of the spectrum to the one of double bond isomer **10** is evident. Thus the structures of the resulting monoketal **14** and the diketal **15** could be established.

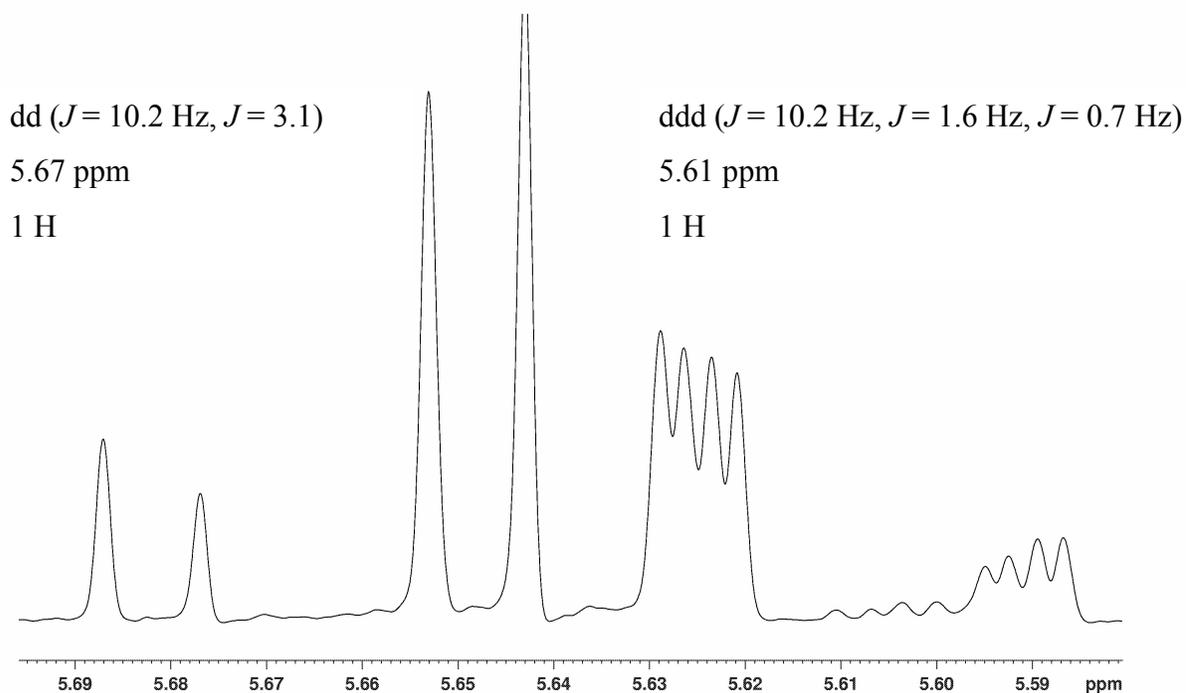
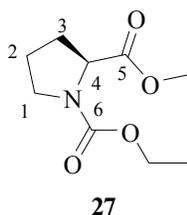


Figure S5 ^1H -NMR spectrum of the obtained diketal **15**

Synthesis of the proline-based oxazaborolidines 21a-d :

(S)-N-(Ethoxycarbonyl)-proline methyl ester (27)



L-Proline (5.00 g, 43.2 mmol) was dissolved in 86 mL of methanol. Potassium carbonate (5.97 g, 43.2 mmol) was added and the mixture was cooled to 0 °C. Then 9 mL (10.3 g, 95.0 mmol) ethyl chloroformate were added slowly. The resulting solution was allowed to warm up to room temperature and was stirred for further 12 h.

The resulting colorless solid was filtered off, the solvent was reduced in vacuo and the remaining colorless oil was transferred to 20 mL of H_2O . Then 25 mL of CH_2Cl_2 were added and the layers were separated. The aqueous layer was extracted with 3 x 10 mL CH_2Cl_2 and the combined

organic layers were dried over MgSO_4 . Concentration under reduced pressure afforded the product as colorless oil (7.62 g, 38 mmol, 87%).

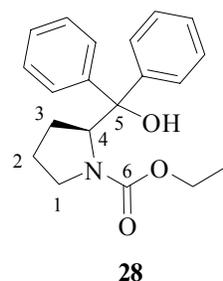
A mixture of rotamers was obtained.

$^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.20 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.27 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.82 -2.33 (m, 8H, 2-H, 3-H), 3.38 -3.67 (m, 4H, 1-H), 3.73 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 4.01 - 4.22 (m, 4H, CH_2CH_3), 4.31 (dd, J = 3.5, J = 8.6 Hz, 1H, 4-H), 4.37 (dd, J = 3.5, J = 8.6 Hz, 1H, 4-H) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ = 14.6 (CH_2CH_3), 14.7 (CH_2CH_3), 23.5, 24.3, 29.9, 30.9 (C-2, C-3), 46.3, 46.7 (C-1), 52.1, 52.2 (OCH_3), 58.8, 59.0 (C-4), 61.2, 61.3 (OCH_2), 154.6, 155.1 (C-6), 173.3, 173.4 (C-5) ppm.

Spectroscopic data were consistent with previously reported data for this compound.⁴

(*S*)-*N*-Ethoxy- α,α -diphenyl-2-pyrrolidinemethanol (**28**)



In an oven dried Schlenk flask 7.36 g (0.30 mol) magnesium turnings were covered with 75 mL of THF. A small amount of bromobenzene (2 mL, 0.02 mol) was added to the mixture and the reaction was started using a heat gun. Then a mixture of 13.8 mL (20.7 g, 0.13 mol) bromobenzene and 25 mL of THF was added dropwise and after complete addition the grey solution was refluxed for further 30 min.

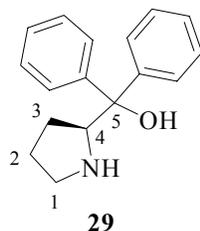
Under an inert gas atmosphere (*S*)-*N*-(ethoxycarbonyl)proline methyl ester (**27**) (7.62 g, 37.8 mmol) was dissolved in 75 mL THF and cooled to 0 °C. The Grignard-solution was added slowly over a period of one hour and the resulting solution was stirred for further 10 h at room temperature. The reaction was hydrolyzed using 50 mL sat. NaHCO_3 solution. After the addition of 100 mL of dichloromethane the layers were separated and the aqueous layer was extracted with 3 x 15 mL CH_2Cl_2 . The combined organic layers were dried over MgSO_4 and concentrated in vacuo. Purification by flash chromatography (2:1 hexanes/ethyl acetate) afforded the product as a colorless solid (3.60 g, 11.1 mmol, 30%).

$^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 0.82$ (b, 1H, 3- H_a), 1.22 (t, $J = 7.2$ Hz, 3H, OCH_2CH_3), 1.43 – 1.56 (m, 1H, 2- H_a), 1.89 – 2.00 (m, 1H, 3- H_b), 2.05 – 2.15 (m, 1H, 2- H_b), 2.95 (m, 1H, 1- H_a), 3.36 – 3.47 (m, 1H, 1- H_b), 4.02 – 4.18 (m, 2H, OCH_2CH_3), 4.92 (dd, $J = 3.8$, $J = 8.8$ Hz, 1H, 4-H), 7.22 – 7.42 (m, 10H, Ph) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): $\delta = 14.6$ (CH_2CH_3), 23.0, 29.7 (C-2, C-3), 47.7 (C-1), 61.9 (OCH_2CH_3), 65.9 (C-4), 81.6 (C-5), 127.1, 127.2, 127.5, 127.6, 127.9, 128.2 (Ph), 143.7 (ArC), 146.4 (C-6) ppm.

Spectroscopic data were consistent with previously reported data for this compound.⁴

(*S*)- α,α -Diphenyl-2-pyrrolidinemethanol (**29**)



(*S*)-*N*-Ethoxy- α,α -diphenyl-2-pyrrolidinemethanol (**28**) (3.60 g, 11.1 mmol) was dissolved in 46 mL of methanol. Potassium hydroxide (7.60 g, 0.13 mol) was added and the resulting solution was refluxed for 60 h. After concentration the resulting yellow oil was transferred to 30 mL H_2O and 30 mL of dichloromethane were added. The layers were separated and the aqueous layer was extracted with 4 x 40 mL CH_2Cl_2 . The combined organic layers were washed with brine, dried over MgSO_4 and concentrated in vacuo. After recrystallization from 3 mL of heptane 2.60 g (0.010 mol, 86%) of a colorless solid were obtained.

$^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 1.50$ – 1.81 (m, 4H, 2-H, 3-H), 2.88 – 3.08 (m, 2H, 1-H), 4.25 (t, $J = 7.6$ Hz, 1H, 4-H), 7.12 – 7.60 (m, 10H, Ph) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): $\delta = 25.5$, 26.3 (C-2, C-3), 46.8 (C-1), 64.5 (C-4), 77.1 (C-5), 125.6, 125.9, 126.3, 126.4, 128.0, 128.2 (Ph), 145.4 (ArC), 148.2 (ArC) ppm.

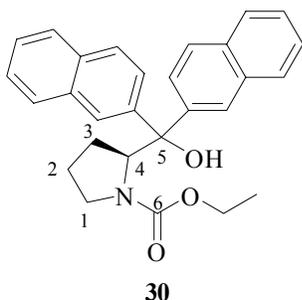
$[\alpha]_D^{20} = -52.1$ ($c = 0.261$, MeOH) [Lit.:⁵ -54.3 ($c = 0.261$, MeOH)]

Spectroscopic data were consistent with previously reported data for this compound.⁴

**(S)-Ethyl 2-(hydroxydinaphthalen-2-ylmethyl)pyrrolidine-1-carboxylate (30),
(S)-1,1-Di(naphthalen-2-yl)tetrahydropyrrolo[1,2-c]oxazol-3(1H)-one (31)**

In an oven dried Schlenk flask 0.60 g (24.7 mmol) magnesium turnings were covered with 20 mL of THF. A small amount of 2-bromonaphthalene (0.50 g, 2.40 mmol) in 2 mL of THF was added to the reaction mixture. The reaction was started using one crystal of iodine. Then a mixture of 1.99 g (9.6 mmol) 2-bromonaphthalene and 8 mL of THF was added dropwise and after complete addition the grey solution was refluxed for further three hours.

Then 0.61 g (3.03 mmol) (*S*)-*N*-(ethoxycarbonyl)proline methyl ester (**27**) were dissolved in 30 mL of THF and cooled to 0 °C. Since the Grignard-solution was poorly soluble in cold THF, it was dissolved in hot benzene. The addition of the Grignard-solution was completed after one hour and the mixture was stirred for further 10 h at room temperature. The reaction was hydrolyzed using 10 mL sat. NaHCO₃ solution. After the addition of 20 mL of dichloromethane the layers were separated and the aqueous layer was extracted with 3 x 15 mL CH₂Cl₂. The combined organic layers were dried over MgSO₄ and concentrated in vacuo. Purification by flash chromatography (2:1 hexanes/ethyl acetate) afforded 0.50 g (42%) of a mixture (1:1) of desired product **30** and the cyclic carbamate **31**.

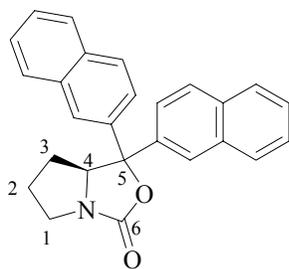


R_f = 0.66 (2:1 hexanes/ethyl acetate, anisaldehyde)

¹H-NMR (300 MHz, CDCl₃): δ = 0.79 (b, 1H, 3-H_a), 1.20 (t, *J* = 6.8 Hz, 3H, OCH₂CH₃), 1.40 – 1.55 (m, 1H, 2-H_a), 2.06 – 2.29 (m, 2H, 2-H_b, 3-H_b), 2.90 – 3.04 (m, 1H, 1-H_a), 3.36 – 3.50 (m, 1H, 1-H_b), 4.02 – 4.18 (m, 2H, OCH₂CH₃), 5.14 (dd, *J* = 4.0, *J* = 8.7 Hz, 1H, 4-H), 7.42 – 7.60 (m, 6H, Ar), 7.72 – 7.92 (m, 8H, Ar) ppm.

¹³C-NMR (75 MHz, CDCl₃): δ = 14.8 (CH₂CH₃), 23.3, 30.0 (C-2, C-3), 48.0 (C-1), 62.2 (OCH₂CH₃), 66.4 (C-4), 82.1 (C-5), 125.4, 126.1, 126.2, 126.3, 126.6, 127.1, 127.3, 127.5, 127.7, 128.0, 128.57, 128.59 (Ph), 132.78, 132.82, 133.0, 141.3 (ArC), 143.8 (C-6) ppm.

Spectroscopic data were consistent with previously reported data for this compound.⁴

**31**

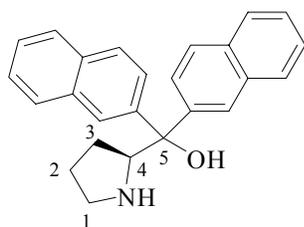
$R_f = 0.66$ (2:1 hexanes/ethyl acetate, anisaldehyde)

$^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 1.13 - 1.22$ (m, 1H, 3- H_a), 1.72 – 1.78 (m, 1H, 3- H_b), 1.85 – 1.93 (m, 1H, 2- H_a), 1.93 – 2.01 (m, 1H, 2 H_b), 3.27 – 3.33 (m, 1H, 1- H_a), 3.73 – 3.80 (m, 1H, 1- H_b), 4.77 (dd, $J = 5.5$, $J = 10.5$ Hz, 1H, 4-H), 7.31 (dd, $J = 1.9$, $J = 8.6$ Hz, 1H, Ar), 7.45 – 7.52 (m, 4H, Ar), 7.62 (dd, $J = 2.1$, $J = 8.6$ Hz, 1H, Ar), 7.50 – 7.88 (m, 6H, Ar), 8.02 (d, $J = 2.1$ Hz, 1H, Ar), 8.10 (d, $J = 2.1$ Hz, 1H, Ar) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): $\delta = 25.0$, 29.1 (C-2, C-3), 46.1 (C-1), 68.7 (C-4), 86.2 (C-5), 123.8, 124.0, 124.2, 124.5, 124.9, 126.5, 126.6, 126.7, 127.5, 127.6, 128.2, 128.4, 128.5, 128.7 (Ph), 132.6, 132.8, 132.9, 133.0, 137.5, 140.1 (ArC), 160.4 (C-6) ppm.

Spectroscopic data were consistent with previously reported data for this compound.⁶

(*S*)- α,α -Di-2-naphthyl-2-pyrrolidinemethanol (**32**)

**32**

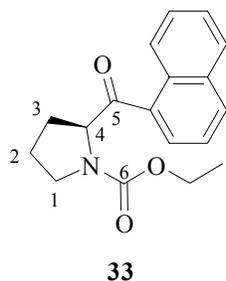
The mixture of (*S*)-1,1-di(naphthalen-2-yl)tetrahydropyrrolo[1,2-c]oxazol-3(1*H*)-one **31** and (*S*)-ethyl 2-(hydroxydinaphthalen-2-ylmethyl)pyrrolidine-1-carboxylate **30** (0.38 g, 1.24 mmol) was dissolved in 10 mL of methanol and an excess of potassium hydroxide (2.40 g, 0.04 mol) was added. The mixture was stirred for 15 h at room temperature, methanol was distilled off and the residue was dissolved in 5 mL of dichloromethane. Water was added (5 mL), the layers were separated and the organic layer was dried over MgSO_4 . After concentration in vacuo 0.27 g (0.76 mmol, 80%) of desired product was isolated as a colorless solid.

$^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.60 – 1.83 (m, 5H, 2-H, 3-H, NH), 2.97 – 3.13 (m, 2H, 1-H), 4.51 (t, J = 7.5, 1H, 4-H), 4.80 – 5.00 (br, 1H, OH), 7.38 – 7.50 (m, 4H, Ar), 7.58 (dd, J = 1.8, J = 8.7 Hz, 1H, Ar), 7.66 – 7.77 (m, 5H, Ar), 7.82 – 7.88 (m, 2H, Ar), 8.09 – 8.11 (m, 2H, Ar) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ = 25.6, 26.5 (C-2, C-3), 46.9 (C-1), 64.0 (C-4), 77.2 (C-5), 123.8, 124.0, 124.4, 125.3, 125.6, 125.8, 125.9, 126.1, 127.5, 127.7, 128.1, 128.2, 128.3, (Ph), 132.20, 132.23, 133.1, 133.2, 142.6, 145.3, (ArC) ppm.

Spectroscopic data were consistent with previously reported data for this compound.⁷

(*S*)-Ethyl 2-(1-naphthoyl)pyrrolidine-1-carboxylate (**33**)



In an oven dried Schlenk flask 4.3 g (0.18 mol) magnesium turnings were covered with 30 mL of THF. A small amount of 1-bromonaphthalene (0.5 g, 2.41 mmol) in 3 mL of THF was added to the reaction mixture. The reaction was started using one crystal of iodine. Then a mixture of 17.8 g (86.0 mmol) 1-bromonaphthalene and 20 mL of THF was added drop wise and after complete addition the grey solution was refluxed for further three hours.

Then 4.43 g (22.0 mmol) (*S*)-*N*-(ethoxycarbonyl)proline methyl ester **27** were dissolved in 30 mL of THF and cooled to 0 °C. Since the obtained Grignard-solution was poorly soluble in cold THF, it was dissolved in hot benzene. The addition of the Grignard-solution was completed after one hour and the mixture was stirred for further 14 h at room temperature. The reaction was hydrolyzed using 100 mL sat. NaHCO_3 solution. After the addition of 100 mL of dichloromethane the layers were separated and the aqueous layer was extracted with 3 x 25 mL CH_2Cl_2 . The combined organic layers were dried over MgSO_4 and concentrated in vacuo. Purification by flash chromatography (1:1 hexanes/ethyl acetate) afforded 1.45 g (22%) of monoarylated product **33**.

R_f = 0.66 (1:1 hexanes/ethyl acetate, anisaldehyde)

Obtained was a mixture of two rotamers.

$^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.12 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 1.31 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 1.88 – 2.27 (m, 8H, 2-H, 3-H), 3.52 – 3.66 (m, 2H, 1-H), 3.72 – 3.83 (m, 2H, 1-H), 4.11 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 4.20 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 5.26 (dd, J = 3.7, J = 8.9 Hz, 1H, 4-H), 5.32 (dd, J = 3.7, J = 8.9 Hz, 1H, 4-H), 7.45 - 7.62 (m, 6H, Ar), 7.82 - 8.04 (m, 6H, Ar), 8.40 (d, J = 8.5 Hz, 1H, Ar), 8.45 (d, J = 8.5 Hz, 1H, Ar) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ = 14.6, 14.8 (CH_2CH_3), 23.3, 24.2, 29.3, 30.4 (C-2, C-3), 46.8, 47.3 (C-1), 61.3, 61.4 (OCH_2CH_3), 64.0, 64.5 (C-4), 124.3, 124.5, 125.3, 125.4, 126.5, 126.7, 127.0, 127.5, 127.9, 128.0, 128.4, 128.5, 130.5, 132.3, 132.5, 133.8, 133.9, 134.8, 135.1 (Ar), 154.6, 155.4 (C-6), 202.4, 203.1 (C-5) ppm.

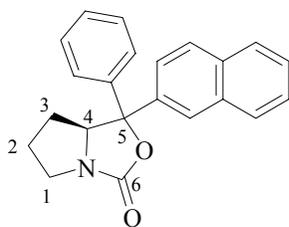
HRMS (ESI): calcd. for $\text{C}_{18}\text{H}_{19}\text{NO}_3\text{Na}^+$, 320.1263 found 320.1257.

MS (APCI) m/z : 298.1 [$\text{M} + \text{H}$] $^+$, 252.1 [$\text{M} - \text{C}_2\text{H}_5\text{O}$], 224.1 [$\text{M} - \text{COOC}_2\text{H}_5$], 208.1, 155.0, 142.1, 127.0, 114.0, 98.0, 70.1.

FT-IR (ATR): ν = 2979 (w), 1683 (s), 1419 (m), 1380 (w), 1343 (m), 1231 (w), 1175 (m), 1120 (m), 1004 (w), 948 (m), 887 (m), 777 (m), 740 (m) cm^{-1} .

$$[\alpha]_D^{20} = -25.0 \text{ (c = 1.024, CH}_2\text{Cl}_2\text{)}$$

(7a*S*)-1-(naphthalen-2-yl)-1-phenyltetrahydropyrrolo[1,2-*c*]oxazol-3(1*H*)-one (34)



34

In an oven dried Schlenk flask 88.5 mg (3.64 mmol) magnesium turnings were covered with 10 mL of THF. A small amount of bromobenzene (0.03 mL, 0.05 g, 0.30 mmol) in 1 mL of THF was added to the reaction mixture. The reaction was started using one crystal of iodine. In the following a mixture of 0.16 mL (0.24 g, 1.50 mmol) bromobenzene and 5 mL of THF was added dropwise and after complete addition the grey solution was refluxed for further three hours.

Then 0.27 g (0.91 mmol) (*S*)-Ethyl 2-(1-naphthoyl)pyrrolidine-1-carboxylate **33** were dissolved in 5 mL of THF and cooled to 0 °C. The obtained Grignard-solution was added slowly over a period of one hour and the resulting solution was stirred for further 10 h at room temperature.

The reaction was hydrolyzed using 10 mL sat. NaHCO₃ solution. After the addition of 10 mL of dichloromethane the layers were separated and the aqueous layer was extracted with 3 x 5 mL CH₂Cl₂. The combined organic layers were dried over MgSO₄ and concentrated in vacuo. Purification by flash chromatography (2:1 hexanes/ethyl acetate) afforded the product as a colorless solid (0.10 g, 0.30 mmol, 33%).

R_f = 0.6 (2:1 hexanes/ethyl acetate, anisaldehyde)

¹H-NMR (300 MHz, CDCl₃): δ = 0.84 – 1.01 (m, 1H, 3-H_a), 1.28 – 1.40 (m, 1H, 3-H_b), 1.72 – 1.96 (m, 2H, 2-H), 3.33 – 3.45 (m, 1H, 1-H_a), 3.72 – 3.85 (m, 1H, 1-H_b), 4.95 (dd, *J* = 5.4, *J* = 10.9 Hz, 1H, 4-H), 7.25 – 7.33 (m, 4H, Ar), 7.39 – 7.45 (m, 3H, Ar), 7.57 (dd, *J* = 7.3, *J* = 8.3 Hz, 1H, Ar), 7.85 – 7.90 (m, 2H, Ar), 8.02 (d, *J* = 2.1 Hz, 1H, Ar), 8.08 (dd, *J* = 1.3, *J* = 7.4 Hz, 1H, Ar) ppm.

¹³C-NMR (75 MHz, CDCl₃): δ = 24.3, 28.5 (C-2, C-3), 46.4 (C-1), 69.2 (C-4), 86.2 (C-5), 124.4, 125.2, 125.5, 125.6, 125.9, 127.0, 128.8, 128.9, 129.1, 129.2 (Ar), 129.4, 134.1, 135.5, 142.6 (ArC), 160.1 (C-6) ppm.

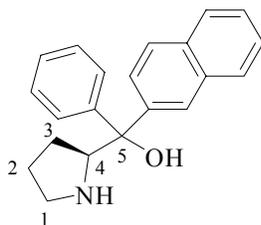
HRMS (ESI): calcd. for C₂₂H₁₉NO₂Na⁺ 352.1313, found 352.1311.

MS (ESI) *m/z*: 352.1 [M + Na]⁺, 330.1 [M + H]⁺, 286.2, 269.1, 191.1, 165.1.

FT-IR (ATR): ν = 3059 (w), 2975 (w), 2114 (w), 1748 (s), 1598 (w), 1509 (w), 1448 (w), 1376 (m), 1230 (m), 1049 (m), 962 (m), 802 (m), 778 (m) cm⁻¹.

$$[\alpha]_D^{20} = -8.66 \text{ (c = 0.138, CH}_2\text{Cl}_2\text{)}$$

(S)-α,α-(1-Naphthyl)-phenyl-2-pyrrolidinemethanol (35)



35

(7a*S*)-1-(Naphthalen-2-yl)-1-phenyltetrahydropyrrolo[1,2-*c*]oxazol-3(1*H*)-one **34** (0.07 g, 0.21 mmol) was dissolved in 3 mL of methanol and an excess of potassium hydroxide (0.50 g, 9.00

mmol) was added. The mixture was refluxed for 15 h, methanol was distilled off and the residue was dissolved in 3 mL of dichloromethane. Water was added (3 mL), the layers were separated and the organic layer was dried over MgSO₄. After concentration in vacuo 0.06 g (0.20 mmol, 93%) of desired product was isolated as a yellow oil.

¹H-NMR (300 MHz, CDCl₃): δ = 1.62 – 2.06 (m, 4H, 2-H, 3-H), 2.82 – 2.94 (m, 1H, 1-H_a), 3.01 - 3.13 (m, 1H, 1-H_b), 4.20 – 4.29 (m, 1H, 4-H), 7.12 – 7.16 (m, 1H, Ar), 7.23 – 7.37 (m, 4H, Ar), 7.48 – 7.52 (m, 3H, Ar), 7.76 – 7.81 (m, 3H, Ar), 8.50 (br, 1H, Ar) ppm.

¹³C-NMR (75 MHz, CDCl₃): δ = 25.8, 27.5 (C-2, C-3), 46.6 (C-1), 65.8 (C-4), 79.4 (C-5), 124.2, 124.3, 125.1, 125.4, 125.9, 126.3, 127.9, 128.46, 128.50 (Ph), 131.7, 134.8, 140.1, 147.7 (ArC) ppm.

HRMS (ESI): calcd. for C₁₈H₁₉NO₃, 304.1701 found 304.1696 [M + H]⁺.

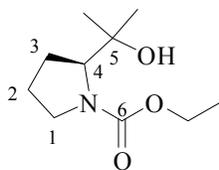
MS (ESI) *m/z*: 304.17 [M + H]⁺, 286.16 [M – OH].

FT-IR (ATR): ν = 3589 (s), 3205 (s), 3058 (m), 2960 (s), 2670 (m), 1505 (w), 753 (m) cm⁻¹.

$$[\alpha]_D^{20} = -20.0 \text{ (c = 0.04, CH}_2\text{Cl}_2\text{)}$$

mp.: 134 °C

(*S*)-*N*-Ethoxy- α,α -dimethyl-2-pyrrolidinemethanol (**36**)



36

In an oven dried Schlenk flask 1.94 g (0.08 mol) magnesium turnings were covered with 10 mL of diethyl ether. A small amount of methyl iodide (0.31 mL, 0.71 g, 5.00 mmol) was added to the mixture and the reaction was started using a heat gun. In the following a mixture of 2.18 mL (4.97 g, 35.0 mol) methyl iodide and 15 mL of Et₂O was added drop wise and after complete addition the colorless solution was refluxed for further 30 minutes.

Under an inert gas atmosphere (*S*)-*N*-(ethoxycarbonyl)proline methyl ester **27** (1.00 g, 4.95 mmol) was dissolved in 20 mL Et₂O and cooled to 0 °C. The obtained Grignard-solution was added slowly over a period of one hour and the resulting solution was stirred for further 10 h at room temperature. The reaction was hydrolyzed using 20 mL sat. NaHCO₃ solution. After the addition of 20 mL of dichloromethane the layers were separated and the aqueous layer was extracted with

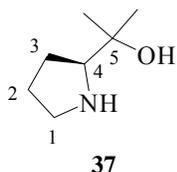
3 x 10 mL CH₂Cl₂. After drying over MgSO₄ concentration afforded 1.00 g (4.95 mmol, 100%) of the desired product as yellow oil.

¹H-NMR (300 MHz, CDCl₃): δ = 1.07 (s, 3H, Me), 1.17 (s, 3H, Me), 1.27 (t, *J* = 7.1, 3H, OCH₂CH₃), 1.49 – 2.20 (m, 4H, 2-H, 3-H), 3.15 – 3.27 (m, 1H, 1-H_a), 3.66 – 3.79 (m, 1H, 1-H_b), 3.89 (t, *J* = 7.4, 1H, 4-H), 4.15 (q, *J* = 7.1, 2H, OCH₂CH₃), 5.73 (br, 1H, OH) ppm.

¹³C-NMR (75 MHz, CDCl₃): δ = 14.8 (OCH₂CH₃), 23.3, 24.4 (C-2, C-3), 27.8, 29.2 (Me), 48.2 (C-1), 61.9 (OCH₂CH₃), 67.9 (C-4), 73.8 (C-5), 158.5 (C-6) ppm.

Spectroscopic data were consistent with previously reported data for this compound.⁸

(*S*)- α,α -Dimethyl-2-pyrrolidinemethanol (**37**)



(*S*)-*N*-Ethoxy- α,α -dimethyl-2-pyrrolidinemethanol **36** (0.50 g, 2.48 mmol) was dissolved in 30 mL of methanol and an excess of potassium hydroxide (4.48 g, 0.08 mol) was added. The mixture was refluxed for 15 h, methanol was distilled off and the residue was dissolved in 5 mL of dichloromethane. Water was added (5 mL), the layers were separated and the organic layer was dried over MgSO₄. After concentration in vacuo 0.10 g (0.77 mmol, 32%) of desired product was isolated as a yellow oil.

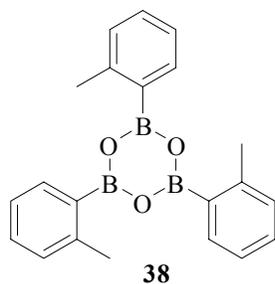
¹H-NMR (300 MHz, CDCl₃): δ = 1.09 (s, 3H, Me), 1.12 (s, 3H, Me), 1.50 - 1.80 (m, 4H, 2-H, 3-H), 2.8 – 3.0 (m, 3H, 1-H, 4-H) ppm.

¹³C-NMR (75 MHz, CDCl₃): δ = 13.9, 14.9 (C-2, C-3), 15.3, 17.5 (Me), 35.8 (C-1), 55.6 (C-4), 59.2 (C-5) ppm.

Spectroscopic data were consistent with previously reported data for this compound.⁹

Tri(*o*-tolyl)boroxin (**38**)

o-Tolylboronic acid (0.92 g, 6.80 mmol) was dissolved in 20 mL of toluene, heated to 150 °C and was directly distilled off via a claisen bridge. This procedure was repeated three times. The favored product was obtained as a colorless solid (0.65 g, 1.84 mmol, 81%).



$^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 2.83$ (s, 3H, Me) 7.24 – 7.32 (m, 2H), 7.44 (td, $J = 7.5$, $J = 1.6$ Hz, 1H), 8.20 (dd, $J = 7.3$, $J = 1.3$ Hz, 1H) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): $\delta = 23.1$, 125.2, 130.6, 132.2, 137.2, 146.3 ppm.

Spectroscopic data were consistent with previously reported data for this compound.¹⁰

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